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Regulations Amending the Food and Drug Regulations (Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19): SOR/2021-45

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FOOD AND DRUGS ACT

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His Excellency the Administrator of the Government of Canada in Council, on the recommendation of the Minister of Health, pursuant to section 30 ^a of the *Food and Drugs Act* ^b, makes the annexed *Regulations Amending the Food and Drug Regulations (Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19)*.

Regulations Amending the Food and Drug Regulations (Interim Order Respecting the Importation, Sale and Advertising of Drugs

for Use in Relation to COVID-19)

Amendments

1 Subsection C.01.001(1) of the *Food and Drug Regulations* ¹ is amended by adding the following in alphabetical order:

COVID-19

means the coronavirus disease 2019; (*COVID-19*)

COVID-19 drug

means a drug, other than a veterinary health product, that is manufactured, sold or represented for use in relation to COVID-19; (*drogue contre la COVID-19*)

ISAD Interim Order

means the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19* made by the Minister on September 16, 2020 and published in Part I of the *Canada Gazette* on October 3, 2020; (*arrêté d'urgence IVPD*)

2 (1) Section C.01.014.21 of the Regulations is amended by adding the following after subsection (1):

(1.1) The Minister may, at any time, impose terms and conditions on a drug identification number assigned for a designated COVID-19 drug, or amend those terms and conditions, if

(a) a notice of compliance was issued under section C.08.004 in respect of

(i) a new drug submission that was filed under section C.08.002 for the designated COVID-19 drug that contains the statement referred to in paragraph C.08.002(2.1)(a), or

(ii) a supplement to a new drug submission referred to in subparagraph (i) that was filed under section C.08.003 for the designated COVID-19 drug; or

(b) a notice of compliance was issued under section C.08.004 in respect of one of the following that was filed for the designated COVID-19 drug on the basis of a direct or indirect comparison to another designated COVID-19 drug referred to in paragraph (a):

(i) a new drug submission under section C.08.002,

(ii) an abbreviated new drug submission under section C.08.002.1, or

(iii) a supplement to a new drug submission or abbreviated new drug submission under section C.08.003.

(2) Subsection C.01.014.21(3) of the Regulations is replaced by the following:

(3) The following definitions apply in this section.

Class B opioid

means a drug set out in Part B of the *List of Opioids*, published by the Government of Canada on its website, as amended from time to time.
(*opioïde de catégorie B*)

designated COVID-19 drug

has the same meaning as in section C.08.001.1. (*drogue désignée contre la COVID-19*)

3 Section C.01A.005 of the Regulations is renumbered as subsection C.01A.005(1) and is amended by adding the following:

(2) In addition to the information and documents referred to in subsection (1), a person who submits an application for an establishment licence that relates to one or more activities set out in Table I to section C.01A.008 to be

carried out in respect of a category of drugs set out in Table II to that section that includes a COVID-19 drug may include a statement to that effect in the application.

4 Section C.01A.006 of the Regulations is amended by adding the following after subsection (1):

(1.1) In addition to the information and documents referred to in subsection (1), a person who submits an application to amend an establishment licence that relates to one or more activities set out in Table I to section C.01A.008 to be carried out in respect of a category of drugs set out in Table II to that section that includes a COVID-19 drug may include a statement to that effect in the application.

5 Paragraph C.01A.007(2)(a) of the French version of the Regulations is replaced by the following:

a) qu'une inspection soit effectuée aux heures normales de bureau de tout bâtiment visé aux alinéas C.01A.005(1)g) ou h);

6 (1) Subsection C.01A.008(1) of the Regulations is replaced by the following:

C.01A.008 (1) Subject to subsection (1.1) and section C.01A.010, the Minister shall, on receipt of the information and material referred to in sections C.01A.005 to C.01A.007, issue or amend an establishment licence.

(1.1) The Minister shall, in determining whether he or she has received the information and material referred to in sections C.01A.005 to C.01A.007 in relation to an application referred to in subsection C.01A.005(2) or C.01A.006(1.1) that contains the statement referred to in the applicable subsection, also take into consideration the public health need related to COVID-19.

(2) Subsection C.01A.008(4) of the Regulations is replaced by the following:

(4) When issuing an establishment licence, the Minister may impose terms and conditions on the establishment licence respecting

(a) the tests to be performed in respect of a drug, and the equipment to be used, to ensure that the drug is not unsafe for use; and

(b) any other matters necessary to prevent injury to the health of consumers, including conditions under which drugs are fabricated, packaged/labelled or tested.

7 Paragraph C.01A.011(1)(a) of the Regulations is replaced by the following:

(a) the requirements of the establishment licence; and

8 Section C.01A.012 of the Regulations is replaced by the following:

C.01A.012 (1) The Minister may amend the terms and conditions of an establishment licence that are imposed under subsection C.01A.008(4) if the Minister believes on reasonable grounds that an amendment is necessary to prevent injury to the health of the consumer.

(2) The Minister shall give at least 15 days notice in writing to the holder of the establishment licence of the proposed amendment, the reasons for it and its effective date.

9 The Regulations are amended by adding the following after section C.01A.012:

C.01A.012.1 (1) Despite subsection C.01A.008(4), the Minister may, at any time, including when issuing an establishment licence, impose terms and conditions on an establishment licence that is issued or amended under

section C.01A.008 on the basis of an application referred to in subsection C.01A.005(2) or C.01A.006(1.1) that contains the statement referred to in the applicable subsection.

(2) For greater certainty, terms and conditions that may be imposed under subsection (1) are not limited to those that may be imposed under subsection C.01A.008(4).

C.01A.012.2 The Minister may, at any time, amend terms or conditions that are imposed on an establishment licence under subsection C.01A.012.1(1).

10 Paragraph C.01A.013(a) of the Regulations is replaced by the following:

(a) there is any change to the information referred to in any of paragraphs C.01A.005(1)(a), (b) and (e) to (i); or

11 The portion of section C.01A.017.1 of the Regulations before paragraph (a) is replaced by the following:

C.01A.017.1 The Minister may suspend an establishment licence in respect of any or all matters indicated in subsection C.01A.008(2) if, after the Minister has, under section 21.31 of the Act, ordered the licensee to conduct an assessment in order to provide evidence establishing that the licensee's buildings, equipment or practices and procedures, as the case may be, continue to meet the requirements referred to in paragraph C.01A.005(1)(l), subparagraph C.01A.005(1)(m)(ii) or (iii) or paragraph C.01A.005(1)(o),

12 Section C.02.019 of the Regulations is amended by adding the following after subsection (4):

(4.1) Subsections (1) and (2) do not apply to a distributor or importer of a COVID-19 drug if it is the subject of a written request made under section C.04.015.

13 Section C.08.001.1 of the Regulations is amended by adding the following in alphabetical order:

designated COVID-19 drug means a new drug for which the purpose and conditions of use recommended by the manufacturer relate to COVID-19;
(*drogue désignée contre la COVID-19*)

14 (1) Paragraph C.08.002(2)(o) of the Regulations is replaced by the following:

(o) in the case of a new drug for human use other than a designated COVID-19 drug, an assessment as to whether there is a likelihood that the new drug will be mistaken for another drug for which a drug identification number has been assigned due to a resemblance between the brand name that is proposed to be used in respect of the new drug and the brand name, common name or proper name of the other drug.

(2) Section C.08.002 of the Regulations is amended by adding the following after subsection (2):

(2.1) A manufacturer may file, for a designated COVID-19 drug, a new drug submission that does not meet the requirements set out in paragraphs (2) (g) and (h) if the submission contains

(a) a statement that the submission contains evidence to establish that the requirement set out in paragraph (b) is met; and

(b) sufficient evidence to support the conclusion that the benefits associated with the designated COVID-19 drug outweigh the risks for the purpose and under the conditions of use recommended, with

consideration given to the uncertainties relating to those benefits and risks as well as the public health need related to COVID-19.

(2.2) A manufacturer may file, for a designated COVID-19 drug for human use, a new drug submission that does not meet the requirements set out in paragraph (2)(j.1) if the submission contains a draft of every label to be used in connection with the designated COVID-19 drug, including any package insert and any document that is provided on request and that sets out supplementary information on the use of the designated COVID-19 drug.

(2.3) If, at the time a new drug submission is filed for a designated COVID-19 drug, the manufacturer is unable to provide the Minister with information or material referred to in any of paragraphs (2)(e) to (k), (m) and (n) or in paragraph (2.1)(b) or subsection (2.2) or that information or material is incomplete, the manufacturer shall provide the Minister, at that time, with a plan that specifies how and when the manufacturer will provide the Minister with the missing information or material.

(2.4) Subsections (2.1) to (2.3) apply if

(a) the new drug submission contains a statement that the submission is for a designated COVID-19 drug; and

(b) the purpose and conditions of use specified in the new drug submission in respect of the designated COVID-19 drug relate only to COVID-19 and the submission contains a statement to that effect.

(2.5) Subsections (2.1) to (2.3) do not apply if the manufacturer is seeking a notice of compliance for a designated COVID-19 drug on the basis of a direct or indirect comparison between the designated COVID-19 drug and another designated COVID-19 drug.

15 The Regulations are amended by adding the following after section C.08.003:

C.08.003.01 (1) The following definitions apply in this section.

submission

means

- (a)** a new drug submission that is filed under section C.08.002;
- (b)** an extraordinary use new drug submission that is filed under section C.08.002.01;
- (c)** an abbreviated new drug submission that is filed under section C.08.002.1; or
- (d)** an abbreviated extraordinary use new drug submission that is filed under section C.08.002.1. (*présentation*)

supplement

means a supplement to a submission that is filed under section C.08.003. (*supplément*)

(2) Despite sections C.08.002, C.08.002.01, C.08.002.1 and C.08.003 and subject to subsection (3), the manufacturer of a new drug is not permitted to file a submission or supplement for the new drug on the basis of a direct or indirect comparison to any new drug in respect of which an authorization was issued under the ISAD Interim Order.

(3) Subsection (2) does not prevent the manufacturer of a new drug from filing a submission or supplement for the new drug on the basis of a direct or indirect comparison to another new drug in respect of which an authorization was issued under the ISAD Interim Order if

- (a)** a notice of compliance is issued under section C.08.004 or C.08.004.01 in respect of a submission or supplement for that other new drug; and

(b) the comparison is in respect of the matters that were approved by the notice of compliance.

16 Section C.08.004.1 of the Regulations is amended by adding the following after subsection (1):

(1.1) For the purposes of the definition *innovative drug* in subsection (1), a medicinal ingredient is not considered to be approved in a drug by reason of the Minister having issued or amended an authorization under the ISAD Interim Order in respect of a COVID-19 drug that contains the medicinal ingredient.

17 The Regulations are amended by adding the following after section C.08.009:

Pre-positioning of Designated COVID-19 Drugs

C.08.009.01 The following definitions apply in sections C.08.009.03 to C.08.009.05.

Chief Public Health Officer means the Chief Public Health Officer appointed under subsection 6(1) of the *Public Health Agency of Canada Act*.
(*administrateur en chef de la santé publique*)

foreign regulatory authority means a government agency or other entity outside Canada that has a legal right to control the manufacturing, use or sale of drugs within its jurisdiction and that may take enforcement action to ensure that drugs marketed within its jurisdiction comply with the applicable legal requirements. (*autorité réglementaire étrangère*)

C.08.009.02 Sections C.08.009.03 to C.08.009.05 apply in respect of a designated COVID-19 drug if the following conditions are met:

(a) a notice of compliance has not been issued under section C.08.004 or C.08.004.01 in respect of the designated COVID-19 drug; and

(b) Her Majesty in right of Canada has entered into a contract for the procurement of the designated COVID-19 drug.

C.08.009.03 (1) The holder of an establishment licence may import a designated COVID-19 drug if the following conditions are met:

(a) the Chief Public Health Officer provides the Minister with

(i) information indicating that

(A) the designated COVID-19 drug is the subject of a new drug submission that was filed under section C.08.002, or

(B) an application has been submitted to a foreign regulatory authority to authorize the sale of the designated COVID-19 drug,

(ii) the name of the designated COVID-19 drug and a description of it,

(iii) the name and contact information of the designated COVID-19 drug's manufacturer,

(iv) information specifying the quantity of the designated COVID-19 drug to be imported,

(v) the name and contact information of any holder of an establishment licence who is proposed to be an importer of the designated COVID-19 drug, and

(vi) the civic address of the place where the designated COVID-19 drug will be stored after importation;

(b) the holder provides the Minister with

(i) the name and contact information of each fabricator, packager/labeller and tester of the designated COVID-19 drug and the civic address of each building at which the designated COVID-19

drug will be fabricated, packaged/labelled or tested, specifying for each building

(A) the activities referred to in Table I to section C.01A.008 that apply to the designated COVID-19 drug,

(B) the categories referred to in Table II to that section that apply to the designated COVID-19 drug, and

(C) for each category, the dosage form classes, if any, and whether the designated COVID-19 drug will be in a sterile form, and

(ii) a certificate from an inspector indicating that each fabricator's, packager/labeller's and tester's buildings, equipment, practices and procedures meet the applicable requirements of Divisions 2 to 4 or, alternatively, other evidence establishing that those requirements are met; and

(c) the holder is one of those specified in the information that the Chief Public Health Officer provides under subparagraph (a)(v).

(2) Paragraph (1)(b) does not apply to the holder of an establishment licence in respect of a building referred to in subparagraph (1)(b)(i) if

(a) the building is listed in the licence; and

(b) the information referred to in clauses (1)(b)(i)(A) to (C) that the holder submitted in respect of the building in their application for the licence under section C.01A.005 or in an application to amend the licence under section C.01A.006, has not changed.

(3) If the conditions set out in subsection (1) are met, the Minister shall send a letter to the Chief Public Health Officer to that effect.

C.08.009.04 Sections A.01.040 and C.01.004.1, subsection C.01A.004(1), section C.01A.006 and Divisions 2 to 4, other than the following provisions, do not apply in respect of the importation, under section C.08.009.03, of a designated COVID-19 drug by the holder of an establishment licence:

- (a) sections C.02.003.1, C.02.004 and C.02.006, as they apply to the storage of the designated COVID-19 drug by the holder;
- (b) subsection C.02.012(1);
- (c) sections C.02.013 and C.02.014;
- (d) section C.02.015, as it applies to the storage and transportation of the designated COVID-19 drug by the holder;
- (e) subsection C.02.021(1), as it applies to the storage of the designated COVID-19 drug by the holder;
- (f) subsection C.02.022(1);
- (g) section C.02.023;
- (h) subsection C.02.024(1);
- (i) section C.03.013; and
- (j) section C.04.001.1, as it applies to the storage of the designated COVID-19 drug by the holder.

C.08.009.05 Despite anything in these Regulations, the holder of an establishment licence may distribute a designated COVID-19 drug that they have imported under section C.08.009.03 if the following conditions are met:

- (a) the Chief Public Health Officer provides the Minister with the name of the designated COVID-19 drug and the civic address of the place where it will be stored after the distribution; and

(b) the designated COVID-19 drug is distributed to a person who will store it at that place.

Transitional Provisions

Interpretation

18 (1) The following definitions apply in this section and in sections 19 to 30:

authorization

means an authorization that was issued under the ISAD Interim Order in respect of a new drug on the basis of

(a) an application submitted under section 3 of the ISAD Interim Order other than an application that was submitted on the basis of a direct or indirect comparison of the new drug to another drug; or

(b) an application submitted under section 4 of the ISAD Interim Order. (*autorisation*)

supplement

means a supplement to a new drug submission that is filed under section C.08.003 of the *Food and Drug Regulations*. (*supplément*)

(2) Unless the context otherwise requires, words and expressions used in this section and in sections 19 to 30 have the meanings assigned by the *Food and Drug Regulations*.

Authorizations

19 (1) Despite subsection 2(1) of the ISAD Interim Order, the manufacturer of a new drug who is the holder of an authorization in respect of the new drug may file a new drug submission under section

C.08.002 of the *Food and Drug Regulations*, or a supplement, for the new drug and subsection C.01.014.1(3) and Division 8 of Part C of those Regulations apply in respect of the submission or supplement.

(2) The authorization is revoked if the manufacturer does not file a new drug submission under section C.08.002 of the *Food and Drug Regulations*, or a supplement, for the new drug within one of the following periods, as applicable:

(a) in the case of an authorization that was issued before the day on which this section comes into force, 90 days after the day on which this section comes into force; or

(b) in the case of an authorization that is issued on or after the day on which this section comes into force, 90 days after the day on which the authorization is issued.

(3) If the manufacturer files a new drug submission under section C.08.002 of the *Food and Drug Regulations*, or a supplement, for the new drug within the applicable period set out in paragraph (2)(a) or (b), the authorization is revoked when one of the following circumstances occurs:

(a) the Minister issues a notice of compliance under section C.08.004 of those Regulations in respect of the submission or supplement;

(b) if the Minister issues a notice to the manufacturer under paragraph C.08.004(1)(b) of those Regulations in respect of the submission or supplement and the manufacturer does not amend the submission or supplement in accordance with subsection C.08.004(2) of those Regulations, the period referred to in subsection C.08.004(2) expires;

(c) the Minister issues a notice to the manufacturer under paragraph C.08.004(3)(b) of those Regulations in respect of the submission or supplement.

20 The *Food and Drug Regulations* — other than the following provisions — do not apply to a new drug in respect of which an authorization was issued to the manufacturer of the new drug if, immediately before the day on which this section comes into force, the authorization was neither suspended nor revoked:

(a) sections A.01.014, A.01.015, A.01.022 to A.01.043, A.01.050, A.01.051 and A.01.060.1 to A.01.068;

(b) sections C.01.004 to C.01.011, C.01.014.9, C.01.014.10, C.01.017 and C.01.019, subsection C.01.020(1) and sections C.01.020.1, C.01.040.3 to C.01.053, C.01.064 to C.01.069 and C.01.401;

(c) the provisions of Divisions 1A and 2 of Part C;

(d) sections C.03.202, C.03.203 and C.03.206 to C.03.209; and

(e) sections C.04.013 to C.04.016, C.04.019 and C.04.020.

21 (1) The drug identification number that was assigned under subsection 7(1) of the ISAD Interim Order in relation to a new drug that is referred to in section 20 continues to be assigned for the distinct combination of dosage form, strength and route of administration of the new drug.

(2) A reference in Divisions 1 and 1A of Part C of the *Food and Drug Regulations* — other than in sections C.01.050, C.01.052, C.01.053 and C.01A.003 — to a drug identification number is deemed to include a reference to the drug identification number that is referred to in subsection (1).

(3) A reference in section C.01A.003 of the *Food and Drug Regulations* to a distributor who holds a drug identification number is deemed to include a reference to the manufacturer who is referred to in section 20.

22 The manufacturer who is referred to in section 20 shall, within 15 days after the day on which the new drug is first sold in Canada, notify the Minister, in writing, of the date of that first sale, unless the manufacturer has already done so under section 8 of the ISAD Interim Order.

23 The manufacturer who is referred to in section 20 shall, within 15 days after the day on which the manufacturer permanently discontinues the sale in Canada of the new drug, notify the Minister, in writing, of the date on which the sale was permanently discontinued, unless the manufacturer has already done so under section 9 of the ISAD Interim order.

24 Despite the definition *drug* in section C.01.014.8 of the *Food and Drug Regulations*, sections C.01.014.9 and C.01.014.10 of those Regulations apply, with any necessary modifications, to the manufacturer who is referred to in section 20 in respect of the new drug.

25 (1) Subject to subsection (2), sections 20 to 24 cease to apply to a new drug that is referred to in section 20 90 days after the day on which this section comes into force.

(2) If the manufacturer who is referred to in section 20 files, for the new drug, a new drug submission under section C.08.002 of the *Food and Drug Regulations* or a supplement, within the period referred to in subsection (1) or has filed such a submission or supplement before the

day on which this section comes into force, sections 20 to 24 cease to apply to the new drug when one of the circumstances referred to in paragraphs 19(3)(a) to (c) occurs.

26 (1) Despite subsection 1(3) of the ISAD Interim Order, for the purposes of the definition *innovative drug* in subsection C.08.004.1(1) of the *Food and Drug Regulations*, a medicinal ingredient is not considered to be approved in a drug by reason of the Minister having issued or amended an authorization under the ISAD Interim Order in respect of a COVID-19 drug that contains the medicinal ingredient.

(2) Subsection (1) ceases to apply on the day on which the ISAD Interim Order ceases to have effect.

Establishment Licences

27 (1) Any terms and conditions of an establishment licence — other than those that are imposed by the Minister under the ISAD Interim Order — are deemed to be imposed by the Minister under subsection C.01A.008(4) of the *Food and Drug Regulations*.

(2) Any terms and conditions of an establishment licence that are imposed by the Minister under the ISAD Interim Order are deemed to be imposed by the Minister under section C.01A.012.1 of the *Food and Drug Regulations*.

28 (1) Despite subsection 26(1) of the ISAD Interim Order, any establishment licence that is referred to in that subsection is not cancelled immediately before the ISAD Interim Order ceases to have effect if the holder of the establishment licence notifies the Minister in writing, before the day on which the ISAD Interim Order ceases to have effect, of their intention to continue to conduct activities in respect of the COVID-19 drug under the establishment licence.

(2) Despite subsection 26(2) of the ISAD Interim Order, any amendment that is referred to in that subsection to an establishment licence continues to have effect after the ISAD Interim Order ceases to have effect if the holder of the establishment licence notifies the Minister in writing, before the day on which the ISAD Interim Order ceases to have effect, of their intention to continue to conduct activities in respect of the COVID-19 drug under the amended establishment licence.

Pre-positioning of Designated COVID-19 Drugs

29 Information and material in respect of a designated COVID-19 drug that were provided under paragraphs 28(1)(a) and (b) or 30(a) of the ISAD Interim Order are deemed to have been provided under, as the case may be, paragraphs C.08.009.03(1)(a) and (b) or C.08.009.05(a) of the *Food and Drug Regulations*.

30 Section C.08.009.05 of the *Food and Drug Regulations* applies, with any necessary modifications, in respect of a designated COVID-19 drug that was imported under section 28 of the ISAD Interim Order.

Coming into Force

31 (1) Subject to subsection (2), these Regulations come into force on the day on which they are registered.

(2) Sections 3 to 5, subsection 6(1), sections 9 to 12, 15 to 17 and 20 to 25, subsection 27(2) and sections 29 and 30 come into force on the day on which the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19*, made by the Minister on September 16, 2020 and published in Part I of the *Canada Gazette* on October 3, 2020, ceases to have effect.

REGULATORY IMPACT ANALYSIS STATEMENT

(This statement is not part of the Regulations.)

Executive summary

Issues

On September 16, 2020, the Minister of Health made the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19* (the ISAD Interim Order or the Interim Order) to create flexibilities in the drug authorization process, allowing their sale, import and distribution to address the COVID-19 immediate public health risk. The Interim Order will expire one year after being made, however, upon expiry all authorizations and licences issued under the Interim Order will also expire. Unless regulations are brought into place to address this gap, critical access to COVID-19 drugs for Canadians may be interrupted or delayed.

Description

These Regulations introduce amendments to the *Food and Drug Regulations* (FDR) to incorporate some of the elective flexibilities related to market authorization, drug establishment licensing, and pre-positioning of COVID-19 drugs that were made available under the Interim Order. The amendments allow for the continued sale of COVID-19 drugs authorized under the Interim Order. The amendments also allow manufacturers of COVID-19 drugs to use these flexibilities even if no application was made under the ISAD Interim Order.

Rationale

These amendments to the FDR are necessary to maintain a mechanism for COVID-19 – related drugs to be authorized under the FDR, and to facilitate expedited access to these drugs by Canadians, while providing adequate oversight and minimizing burden.

This approach is part of a greater Government of Canada response to address the COVID-19 public health need and aligns internationally.

Issues

The *Food and Drug Regulations* (FDR) provide a robust regulatory framework for drugs to be sold on the Canadian market. However, the amplitude of the COVID-19 pandemic and the need to urgently address the associated public health need has challenged this existing framework. Section 30.1 of the *Food and Drugs Act* (the Act) authorizes the Minister of Health (the Minister) to make an interim order if the Minister believes that immediate action is required to deal with a significant risk, direct or indirect, to health or safety.

The *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19* (the ISAD Interim Order or the Interim Order) was made on September 16, 2020, and further approved by the Governor in Council, on September 25, 2020. Its purpose is to provide optional flexibilities to facilitate the expedited authorization of importation, sale and advertising of drugs to be used in the diagnosis, treatment, mitigation or prevention of COVID-19, as well as the pre-positioning of such drugs.

The ISAD Interim Order ceases to have effect one year after it came into effect. After that time, all authorizations will expire, and drug establishment licences (DELs) issued under the FDR, with the flexibilities under the Interim

Order, may be cancelled. The expiration of the ISAD Interim Order without a plan to transition the Interim Order flexibilities into the FDR may result in the following:

Interrupted or delayed access to COVID-19 drugs for Canadians:

- The framework established under the ISAD Interim Order allowed for more flexibility in evidence required to weigh the benefits, risks and uncertainties related to COVID-19 drugs in respect of the public health need related to COVID-19. Manufacturers that want to start the sale, or continue the sale of their COVID-19 drug(s) in Canada after the Interim Order ceases to have effect will have to file a new drug submission (NDS) under the FDR. However, without the flexibilities for COVID-19 drugs, it could take longer for a company to generate sufficient evidence to support an NDS. This would be in addition to the time required for the Minister to review the submission and issue a notice of compliance (NOC) authorizing the sale and advertisement of the drug. This could result in an unmet medical need or a market lapse of the drug.
- Pre-positioning of promising COVID-19 drugs, including vaccines, would no longer be possible. Importation of such drugs would have to wait until the drug is authorized for sale in Canada, delaying Canadians' access to these drugs immediately following authorization.

Disruption in supply chain:

- COVID-19 drugs that are already in the supply chain (e.g. maintained in provincial stockpiles, hospital pharmacies or wholesaler distribution chains) could no longer be legally sold in Canada once the authorizations expire.

Background

Public health need

COVID-19 is the infectious respiratory disease caused by the novel coronavirus, SARS-CoV-2. The outbreak began in Wuhan, China, in December 2019. COVID-19 infection is known to cause respiratory symptoms, fever, cough, shortness of breath, and breathing difficulties. In more severe cases, it can cause pneumonia, severe acute respiratory syndrome, kidney failure, and death.

The World Health Organization declared a global pandemic caused by a coronavirus on March 11, 2020. Combined global efforts and collaboration between governments and pharmaceutical industry continue to contain the pandemic, and to find effective treatments and cures against this disease.

In Canada, COVID-19 is considered a serious health threat with the situation evolving daily. The risk varies between and within communities, but given the number of cases in Canada, the public health risk to Canadians is considered high. Although COVID-19 is understood to be primarily a new human disease, its impacts on animal health are not fully known at this time. However, there have been several reports of human-to-animal transmission of the virus.

At this time, there is an immediate public health need for drugs for use in the diagnosis, treatment, mitigation or prevention of COVID-19, the lack of which is having a significant impact on our health care system.

Health Canada's response

To help address the immediate and significant risk to the health and safety of Canadians posed by COVID-19, and the associated public health need in Canada, the Minister of Health has made a number of interim orders to streamline and facilitate access to drugs, medical devices and foods for a special dietary purpose. The interim orders were made by the Minister

using the power granted under section 30.1 of the *Food and Drugs Act*, and approved by the Governor in Council. This includes the ISAD Interim Order that provides optional, expedited authorization pathways for the importation, sale and advertising of drugs to be used in relation to COVID-19.

Existing regulatory framework under the FDR

Drug product authorization

Prior to selling a new drug in Canada, a manufacturer must obtain authorization in the form of a notice of compliance (NOC) and a drug identification number (DIN). One way to obtain an NOC is to file an NDS under Part C, Division 8 (New Drugs) of the existing *Food and Drug Regulations* (FDR), and have the information on its safety, efficacy and quality reviewed and authorized by the Minister of Health. DINs are assigned at the time the NOC is issued. Generally, it takes many years to develop the drug and generate the information and evidence necessary to satisfy these NDS requirements and thereby obtain an NOC and a DIN.

Drug establishment licensing requirements

A person who conducts a regulated activity with a drug in Canada (i.e. fabrication, packaging and labelling, distribution, wholesaling, importation or testing) must hold a drug establishment licence (DEL) as set out in Part C, Division 1A, unless otherwise specified by the FDR. A valid DEL demonstrates compliance with good manufacturing practices (GMP). GMPs are part of quality assurance and are concerned with both production and quality control. Compliance with GMP requirements contributes to ensuring that drugs are consistently produced and controlled.

Health Canada inspects establishments that conduct activities authorized by a DEL to verify compliance with GMP. When a drug is fabricated, packaged/labelled, or tested outside of Canada, the foreign building where those activities occur must be listed on the Canadian importer's DEL. For the foreign building to be listed on the DEL, it must be shown to be compliant with GMP requirements (as described in Part C, Division 2 of the FDR).

ISAD Interim Order

The ISAD Interim Order is a temporary regulation put in place by the Minister of Health and approved by the Governor in Council to address the current pandemic. It provides elective and flexible drug authorization pathways separate from those existing in the FDR, which enable manufacturers and importers of COVID-19 drugs to obtain expedited authorization for the sale, import, distribution and advertising of drugs that are manufactured, sold or represented for use in relation to COVID-19. These flexible, expedited pathways facilitate access to critical COVID-19 drugs in a way that takes into consideration urgent public health needs related to COVID-19. It also provides an option for establishment licences to be issued in relation to COVID-19 drugs in a more agile manner.

There are three distinct pathways under the Interim Order to facilitate market access for COVID-19 drugs:

- An application pathway for the authorization of COVID-19 drugs that has more flexibility in terms of application requirements and time of filing than that under Part C, Division 8 of the FDR;
- An alternative, shortened application pathway for COVID-19 drugs that have been authorized by a foreign regulatory authority. This pathway

is, however, limited to those drugs that the Minister has added to the *List of foreign drugs in relation to the COVID-19 pandemic*; and

- A mechanism that enables the Minister to expand indications to COVID-19 uses for new drugs that are authorized under the FDR without requiring application on the part of the manufacturer, as long as there is evidence that the benefits of the expanded indication outweigh the risks. This mechanism is, however, limited to those drugs that the Minister has added to the *List of new drugs for expanded indication in relation to the COVID-19 pandemic*.

Comparative applications

Given the global nature of the pandemic, the global supply chain and the accelerated development of COVID-19 drugs, supply issues could be faced for newly authorized drugs. Therefore, provisions within the ISAD Interim Order allow an application for the authorization of a subsequent entry drug (generic or biosimilar) to be filed on the basis of a comparison to a COVID-19 drug, in the event that the innovative COVID-19 drug is not available in sufficient quantities in Canada to address the urgent public health need related to COVID-19 (subsection 3(3)). The Interim Order also contains provisions stipulating that a submission or supplement cannot be filed under the FDR for a new drug, in respect of a COVID-19 claim, based on a direct or indirect comparison to a COVID-19 drug authorized under the Interim Order (section 14).

Post-market requirements

There are post-market regulatory obligations for authorization holders to maintain records and to fulfill terms and conditions (T&Cs). Where a COVID-19 drug is authorized under the ISAD Interim Order, the Minister may impose or amend a term or condition on the authorization at any time

during the life of that authorization. In light of the severity of the COVID-19 pandemic, this allows the Minister to act quickly to gather important safety information or mitigate risk in a timely manner. COVID-19 drugs under the Interim Order are subject to the post-market reporting requirements in the FDR.

Drug establishment licences and good manufacturing practices

The ISAD Interim Order allows DELs to be issued in relation to COVID-19 drugs in a manner that takes into consideration the necessity of addressing the urgent public health need related to COVID-19. The pandemic's impact on global regulators' ability to conduct on-site inspections requires a flexible approach that balances the information submitted in a DEL application, such as evidence of compliance, against the need for access to drugs used in relation to COVID-19. The flexible approach in the ISAD Interim Order maintains adequate product quality oversight through the use of T&Cs to mitigate potential risks to health and safety. T&Cs are imposed, where necessary, to limit the licensed activity to be conducted only in relation to the COVID-19 drug.

COVID-19 drugs authorized under the ISAD Interim Order must be fabricated, packaged/labelled, tested and stored in accordance with the GMP requirements set out in Part C, Divisions 2 to 4 of the FDR. The Interim Order provides flexibility with regard to the sampling requirements for finished product testing for packagers/labellers, importers and/or distributors of COVID-19 drugs. Under the Interim Order, packagers/labellers, importers and distributors may rely on certificates of analysis generated by the foreign fabricator to assess compliance with finished product specifications, and importers and distributors of COVID-19 drugs are required to conduct visual confirmation of identity upon receipt

of the drug on the premises in Canada. Packagers/labellers must conduct identity testing before packaging and confirm identity after packaging/labelling.

Pre-positioning

The ISAD Interim Order also provides a mechanism to allow importation of an unauthorized drug into Canada, in anticipation of its market authorization. Known as pre-positioning, the Interim Order provides the Chief Public Health Officer of the Public Health Agency of Canada (PHAC) with the ability to notify the Minister of a need to pre-position a promising COVID-19 drug in Canada prior to the drug receiving market authorization. This allows the drug to be imported and immediately available locally once the drug is authorized. In order for a drug to be pre-positioned, the Government of Canada has entered into a contract for its procurement, and the manufacturer has filed an application for the drug's authorization in Canada, or abroad with a foreign regulatory authority. The regulator also must determine that the establishment that will import the drug is licensed and has demonstrated the fabrication, packaging, labelling and testing activities related to the drug to be pre-positioned comply with the good manufacturing practices requirements of the FDR.

Conclusion of the Interim Order

Together, these temporary measures help ensure Canadians have timely access to COVID-19 drugs. Without amendments to the FDR, all flexibilities, including authorizations issued under the ISAD Interim Order will cease to have effect one year after the Order was made.

Action in other jurisdictions

Foreign regulators including those in the European Union, Australia and the United States have made use of emergency pathways to authorize COVID-19 – related health products as further outlined in the “Regulatory cooperation and alignment” section.

Objective

These amendments to the FDR will allow for continued and timely access to safe and effective COVID-19 drugs for Canadians by normalizing the review, authorization and oversight of these drugs under the FDR by

- enabling the sale and advertising of COVID-19 drugs that were authorized under the ISAD Interim Order, not including those generic drugs authorized to alleviate shortages, to continue without interruption after the Interim Order ceases to have effect, and once authorized under the FDR;
- enabling both COVID-19 drugs that have been authorized under the ISAD Interim Order and new COVID-19 drugs that have not been authorized under the ISAD Interim Order to seek authorization under the FDR with similar flexibilities as had been provided under the Interim Order, such as rolling submissions and the ability to impose and amend terms and conditions;
- permitting continuity of the post-market regulatory obligations placed on authorization holders, manufacturers and importers after expiration of the ISAD Interim Order;
- continuing to provide a legal pathway that allows the early importation (pre-positioning) of a promising COVID-19 drug, for which a Government of Canada contract for its procurement is in place, prior to that drug receiving market authorization in Canada; and

- enabling the continuity of a flexible approach for DELs that authorizes regulated activities in respect of COVID-19 drugs.

Description

Amendments to the FDR

These regulatory amendments integrate some of the flexibilities from the ISAD Interim Order into the sections of the FDR that concern the authorization of the drug for import, sale and advertising, and the licensing of establishments to conduct activities related to that drug (Part C, Divisions 1, 1A, 2 and 8 of the FDR). From the three product authorization pathways included in the ISAD Interim Order described above, only the first pathway relating to submission flexibilities is carried over in these amendments.

The primary intent of these Regulations is to normalize, under the FDR, the review of COVID-19 drug submissions in a manner similar to the Interim Order. Therefore, while the use of foreign decisions and the expanded indication components of the Interim Order were introduced to address the early phases of the pandemic and the associated urgent public health needs, these are not being renewed through these indefinite amendments to the FDR. Health Canada will continue to collaborate with other regulatory authorities, as well as engage with industry to address the urgent public health need and will take action should issues be identified that represent a significant risk to Canadians and the health care system.

A “COVID-19 drug,” in these FDR amendments, means a drug, other than a natural health product or veterinary health product, that is manufactured, sold or represented for use in relation to COVID-19, and captures drugs that may not be specifically indicated for COVID-19, but are used in the treatment of COVID-19. However, for the purposes of those elements that

deal with the authorization of new drugs, associated terms and conditions and pre-positioning, a new definition of a “designated COVID-19 drug” is introduced to narrow the focus to new drugs for which the purpose and conditions of use recommended by the manufacturer relate to COVID-19. For the purpose of this document, “designated COVID-19 drugs” will continue to be collectively referred to as COVID-19 drugs.

Any COVID-19 drug as defined in section C.08.001.2, would be a “new drug” under section C.08.001 and, as a result, would be subject to the requirements in Part C, Division 8 of the FDR. Manufacturers of COVID-19 drugs, whether previously authorized under the Interim Order or not, may file an NDS making use of the new provisions containing submission flexibilities afforded by these regulatory amendments as set out below.

This approach enables manufacturers who initially obtained an authorization under the ISAD Interim Order to normalize their market authorizations under the FDR, by submitting an NDS with the same data as was included in their Interim Order application, along with any necessary updates.

In the event that a manufacturer of COVID-19 drugs was authorized under the Interim Order based on a foreign decision, that manufacturer must submit the information that they submitted to the foreign regulatory authority as part of their new drug submission under the FDR within the appropriate timeline to continue import and sale. Manufacturers using this pathway under the Interim Order would have attested to having this information.

In the event that the Minister expands a drug's indication to include COVID-19, under the expanded indication mechanism of the Interim Order by including it in the *List of New Drugs for Expanded Indication*, manufacturers are exempted from having to file a supplement to a new drug submission

(SNDS) for the COVID-19 indication under section C.08.003 of the FDR. Once the Interim Order expires, this exemption will cease to have effect, and manufacturers may continue to seek to expand the indication of the drug by filing an SNDS under the FDR.

The flexibilities introduced through these amendments are also available to manufacturers of COVID-19 drugs who had not previously received an authorization under the ISAD Interim Order.

Irrespective of the filing date of the Interim Order application or authorization, all NDSs under the new provisions are assigned a new filing date, aligning the process with other drug submissions under Part C, Division 8, of the FDR.

Since neither the course of the pandemic, nor the evolution of the drugs needed to address the urgency can be predicted at this time, there is no endpoint for these amendments.

Incorporation of submission flexibilities into the NDS pathway

These Regulations afford manufacturers of COVID-19 drugs similar flexibilities to those under the ISAD Interim Order. A flexibility available to all COVID-19 drugs is

- the exemption from the requirement under paragraph C.08.002(2)(o) to conduct an assessment as to whether there is a likelihood that the new drug will be mistaken for another drug due to a resemblance between the brand names, commonly referred to as a look-alike sound-alike assessment.

To access additional flexibilities, manufacturers must include a statement identifying that the submission relates to a COVID-19 drug for which only a COVID-19 indication is sought, pursuant to subsection C.08.002(2.4). These flexibilities are not applicable to COVID-19 drugs that also seek other non –

COVID-19 specific indications, to prevent manufacturers from seeking additional indications that do not address the immediate intent of the urgent public health need (e.g. on a rolling basis). These additional submission flexibilities include

- exemption from the requirements for “detailed reports of the tests made to establish the safety” and “substantial evidence of the clinical effectiveness” of the new drug under paragraphs C.08.002(2)(g) and (h) if the applicant is able to provide sufficient evidence that the benefits of the drug outweigh the risks, taking into account uncertainties as well as the public health need related to COVID-19 (subsection C.08.002(2.1));
- exemption from the requirement under paragraph C.08.002(2)(j.1) to provide a mock-up label if the applicant provides a draft of the label, including any package insert and document provided upon request that sets out supplementary information on use of the drug (subsection C.08.002(2.2)); and
- allowing the filing of incomplete submissions along with a plan for filing the remaining information required for Health Canada to make a decision on the submission (further described below) [subsection C.08.002(2.3)].

Incomplete submission and plan for information (rolling submissions)

To expedite the review process, the ability to file NDSs that are completed as data becomes available, as described in subsection C.08.002(2.3), referred to as rolling submissions, will be carried over from the ISAD Interim Order as part of this amendment. Rolling submissions allow a manufacturer to choose to file an NDS for a new COVID-19 drug without including certain NDS information set out in subsection C.08.002(2.3) as

long as the manufacturer includes a plan identifying the missing parts of the submission, along with timelines for when the outstanding information will be submitted. For reasons outlined below, rolling submissions are not available for drugs based on a comparative submission (i.e. subsequent entry drugs including generic pharmaceuticals or biosimilars).

The first part of the submission must include all applicable forms and other administrative components, in addition to the plan. As with other new drug submissions under Division 8, the filing date refers to the date that the NDS is deemed administratively complete by Health Canada (i.e. once all the elements and forms required for processing are completed and submitted to Health Canada). This date may differ from the date of original receipt should the submission be considered administratively incomplete at that time. Data or information that is subsequently provided will be treated as solicited information under the NDS, and will not change the filing date of the submission.

Sufficient information must be submitted within a reasonable timeframe to enable the Minister to review the NDS based on the requirements, and to render a decision under section C.08.004 of the FDR.

Supplements to NDSs

Manufacturers of existing marketed new drugs, who plan to add a COVID-19 indication, are still required to file an SNDS. Although Health Canada aims to prioritize and expedite the review of such submissions aiming to add a COVID-19 indication, there are different considerations for such drugs when it comes to flexibilities. Since such drugs are already authorized for other indications, are available on the market, and have an established quality, safety and on-market experience, there is an expectation that much of the data is already available, including brand name assessments. Given that the data requirements are limited to the

new indication, manufacturers are expected to be able to file an SNDS without these flexibilities. Consequently, the submission flexibilities outlined above, as well as the ability to file an incomplete submission (rolling submission described above) are not applicable to such SNDSs.

Terms and conditions (T&Cs) on the DIN

Currently under the FDR, the Minister has the authority to impose and amend T&Cs on the authorizations for class B opioids and on establishment licences.

To mitigate any risks associated with uncertainties related to the accelerated development and authorization of COVID-19 drugs, as well as to facilitate continued oversight, these amendments to the FDR carry over the ability, from the ISAD Interim Order, for the Minister to place T&Cs at any time on the DIN of a subset of new COVID-19 drugs. Accordingly, the authorities under subparagraphs C.01.014.21(1)(b)(i) and (ii) are amended to allow the Minister to impose T&Cs on that subset of new drugs for which the manufacturer of the COVID-19 drug made a “statement” under subsection C.08.002(2.1) that uses the flexible safety and efficacy evidentiary requirements of the new drug submission.

Examples of anticipated T&Cs could include specific pharmacovigilance and risk mitigation and management measures, additional quality information, confirmation of effectiveness, and measures for the purpose of preventing or alleviating a shortage.

Similarly, T&Cs could also apply to subsequent SNDSs pursuant to the original NDS that included the “statement” above. Furthermore, terms and conditions are also applicable to any future drugs seeking an NOC on the basis of a comparison to a COVID-19 drug that originally used the submission flexibilities (subparagraphs C.01.014.21(1)(c)(i) and (ii)); thus

ensuring that any post-market commitments that were applicable to the reference product may also be imposed on NOCs issued on the basis of a comparison.

Terms and conditions do not apply to any drugs, including COVID-19 drugs using flexibilities under paragraph C.08.002(2)(o) or under subsection C.08.002(2.2) or C.08.002(2.3), where the manufacturer has not made the statement electing to use the amended pathway in subsection C.08.002(2.1), where the NDS is able to meet the data requirements outlined in paragraphs C.08.002(2)(g) and (h).

Intellectual property consequences

As a consequence of normalizing the review, authorization and oversight of COVID-19 drugs under the FDR, the manufacturers of such drugs may benefit from intellectual property protections that are available upon submitting an NDS or SNDS that results in an NOC [i.e. data protection under section C.08.004.1 of the FDR, protection under the *Patented Medicines (Notice of Compliance) Regulations* (PMNOC Regulations), and protection under the *Certificate of Supplementary Protection* regime]. The amendments do not augment or diminish these existing protections.

The amendments contain one interpretative provision clarifying the impact of an authorization under the ISAD Interim Order on data protection eligibility. Subsection C.08.004.1(1) of the FDR provides that an “innovative drug” is one that contains a medicinal ingredient not previously approved in a drug by the Minister and that is not a variation of a previously approved medicinal ingredient. The amendments introduce language to explain that, for the purpose of the definition of “innovative drug” in subsection C.08.004.1(1) of the FDR, a medicinal ingredient is not considered to be approved in a drug by reason of an authorization under the ISAD Interim Order. This amendment is not intended to change the

scope or current interpretation of “approved” under the existing definition; rather, it explains the intended application of that definition where a medicinal ingredient was used in a drug authorized under the ISAD Interim Order.

Though not introduced for this purpose, the new flexibilities contained in these amendments allow an earlier filing of an NDS, making it easier for manufacturers to file their NDS within the time period specified in paragraphs 106(1)(f) under the *Patent Act* and 6(1)(b) established under the *Certificate of Supplementary Protection Regulations* (CSP Regulations), to be eligible to obtain a Certificate of Supplementary Protection.

Subsequent entry drugs

Under the abbreviated new drug submissions (ANDS) and NDS pathways of the FDR, manufacturers of subsequent entry drugs (generic and biosimilar drugs) can seek an NOC based on demonstrated similarity to an approved reference drug (for example, in the case of generic drugs, a Canadian reference product as defined in section C.08.001.1 of the FDR). This is done by filing a comparative submission that relies, in part, on the previously approved evidence of safety and effectiveness regarding the reference drug. As a result, the subsequent entry manufacturer is permitted to submit a reduced data package in the submission.

While these amendments do not change the framework for approving subsequent entry drugs, they do introduce a number of new flexibilities for NDSs. The flexibilities are provided under new subsections C.08.002(2.1), (2.2) and (2.3) and are intended to permit the filing of an NDS that does not contain the usual information otherwise required by the existing NDS pathway under section C.08.002, in order to enable and expedite the introduction of new COVID-19 drugs in Canada.

The new flexibilities do not extend to subsequent entry drug submissions, as manufacturers are allowed in the FDR to submit a reduced data package for ANDSs and comparative NDSs (e.g. biosimilar submissions). Further, as with other subsequent entry drugs, generic or biosimilar COVID-19 drug submissions can only be filed once the reference product has received an NOC and has been marketed. In view of this, it is anticipated that subsequent entry manufacturers will be in a position to meet applicable requirements under the current ANDS or NDS pathways without the need for additional regulatory flexibilities.

Accordingly, the amendments specify that the flexibilities provided under new subsections C.08.002(2.1), (2.2) and (2.3), do not apply to cases where manufacturers seek a notice of compliance for a COVID-19 drug on the basis of a direct or indirect comparison between that drug and another COVID-19 drug (subsection C.08.002(2.5)). Subsection C.08.002(2.5) is not intended to prevent the filing of a submission that contains new data from clinical trials comparing the efficacy of the new therapy to an existing one (sometimes referred to as non-inferiority trials).

Additional provisions have been introduced in these amendments to address the use of reference products authorized under the Interim Order.

The authorization of a COVID-19 drug under the Interim Order was based on the determination that the evidence provided supports the conclusion that the benefits outweigh the risks associated with the drug, taking into account the uncertainties related to the benefits and risks, as well as the urgent public health need caused by COVID-19. This included weighing the risks of modifying certain requirements for information to support the safety and effectiveness of a drug. Subsequent-entry versions of COVID-19

drugs authorized under the ISAD Interim Order are permitted only to address potential shortages, and any such authorizations expire when the Interim Order ceases to have effect.

It remains inappropriate for manufacturers to seek approval of subsequent entry COVID-19 drugs under the FDR based on a reference product authorized under the modified requirements of the ISAD Interim Order. This is consistent with the usual requirement for approving a subsequent entry drug on the basis of a comparison to a reference product that has received an NOC under the *Food and Drug Regulations*. As a result, these amendments to the FDR also specify that manufacturers of subsequent entry products continue to be prohibited from filing a submission on the basis of a direct or indirect comparison to a COVID-19 drug in respect of which an authorization was issued under the ISAD Interim Order (subsection C.08.003.01(2)). Subsection C.08.003.01(2) is not intended to prevent the filing of a submission because it contains new data from clinical trials comparing the efficacy of the new therapy to an existing one. In addition, the amendments do not prevent the filing of a submission or supplement on the basis of a comparison to a COVID-19 drug that has received an NOC (subsection C.08.003.01(3)). As noted above, the current ANDS and NDS pathways remain available.

Health Canada continues to address shortages through the ISAD Interim Order until it ceases to have effect. Shortages may also be addressed through other mechanisms such as the Access to Drugs in Exceptional Circumstances pathway (Part C, Division 10 of the FDR), the *Interim Order Respecting Drugs, Medical Devices and Foods for a Special Dietary Purpose in relation to COVID-19*, or other interim orders as required on a case-by-case basis.

Drug establishment licensing

The amendments to the FDR maintain a flexible licensing approach for drug establishment licensing for activities related to COVID-19 drugs once the Interim Order expires in recognition that COVID-19 drug and vaccine development will continue beyond 2021. An applicant under section C.01A.005 for a new DEL, or section C.01A.006 for an amendment to an existing DEL, may include a statement in their application that they are seeking a licence for an activity or category of drugs that can be used in relation to COVID-19. Similar to section 21 of the Interim Order, these Regulations require the Minister to consider the public health need related to COVID-19 when making a decision to issue or amend the licence (subsection C.01A.008(1.1)). Specifically, this allows the Minister to balance the information submitted in a DEL application (e.g. evidence of GMP compliance) against the need for access to drugs used in relation to COVID-19. The Minister's broad authority to impose or amend T&Cs on these DELs is also maintained (subsections C.01A.012.1 and C.01A.012.2). This broader T&Cs authority is key to the Minister's ability to review evidence of GMP compliance in a way that complements the flexibilities offered to DEL applicants in the context of the public health situation.

Division 1A (Establishment Licenses) already included an authority for the Minister to apply T&Cs to a DEL. However, it was limited to T&Cs related to tests to be performed on a drug and the equipment to be used, or any other matters necessary to prevent injury to the health of the consumer (subsection C.01A.008(4)). Prior to these amendments, the Regulations (paragraph C.01A.011(1)(a)) further required the DEL holder to comply with the T&Cs of the licence. The Regulations re-enact subsection C.01A.008(4), and amend paragraph C.01A.011(1)(a) and section C.01A.012 so that T&Cs are instead enforceable through section 21.7 of the Act to require the

holder of a therapeutic product authorization to comply with T&Cs, including those imposed on a DEL. This does not change how DEL holders must comply with T&Cs that do not relate to COVID-19.

Good manufacturing practices (GMP)

The modified approach to the confirmatory testing requirement that was introduced in the ISAD Interim Order for COVID-19 drugs, as well as the non-application of certain record-keeping requirements, will not be maintained. Once the Interim Order expires, the testing and record-keeping requirements set out in sections C.02.019 and C.02.020, respectively, will apply with one exception; periodic confirmatory testing requirements in subsections C.02.019(1) and (2) will not apply for biologic drugs that are subject to Health Canada oversight for each lot under section C.04.015 (lot release). This amendment will address a known irritant within the biologic drug industry, by reducing burden associated with confirmatory testing when the drug is subject to Health Canada's lot release program.

The modified confirmatory testing and record keeping requirements in the Interim Order were intended to mitigate the challenges faced by industry during the early stages of the pandemic and facilitate rapid access. At that time, lockdowns and other barriers made it difficult or impossible to establish tests required by section C.02.019 of the Regulations without having an impact on the supply chain, and a modified approach was deemed to be acceptable for a temporary situation.

Pre-positioning

Continuing the pre-positioning framework that was introduced in the ISAD Interim Order maintains a pathway that allows the early importation of a promising COVID-19 drug prior to that drug receiving market authorization

in Canada. The framework requires the person importing a drug for pre-positioning to hold a DEL, but does not require the activity of importation to be licensed on the DEL (section C.08.009.04). Once the drug receives market authorization in Canada, regular DEL requirements apply to subsequent importation and distribution.

As in the ISAD Interim Order, COVID-19 drugs will only be eligible for pre-positioning if the Government of Canada has entered into a contract with the manufacturer to procure it and the Chief Public Health Officer (CPHO) of the Public Health Agency of Canada has notified the Minister of the COVID-19 drug to be pre-positioned.

The CPHO must provide the Minister with information consistent with what is requested under the Interim Order (paragraph C.08.009.03(1)(a)), including information about the drug, indicating that either a submission has been filed under the FDR or with a foreign regulatory authority, as well as information about the facilities where the drug will be stored once imported.

The DEL holder that the CPHO proposes to import a COVID-19 drug must provide evidence demonstrating that foreign buildings for which the COVID-19 drug is fabricated, packaged, labelled, or tested meets GMP requirements, unless the foreign building is already listed on the DEL for the same activity, category of drug, dosage form, and whether or not the drug is sterile (paragraph C.08.009.03(1)(b)).

Transitional provisions

For the purposes of the transitional provisions, “authorization” was defined to only refer to authorizations issued based on an application filed under subsection 3(1) and an application based on a foreign decision, filed under section 4 of the ISAD Interim Order. The ISAD Interim Order permits, under

subsection 3(3), for a drug to be authorized on the basis of comparison if sufficient quantities of the drug are not available in Canada to address the urgent public health need related to COVID-19. As drugs authorized under the Interim Order on a comparative basis to another drug were not seen as suitable for transition to an NOC, the definition of “authorization” for the purpose of transitional provisions intentionally excludes authorizations for applications based on a direct or indirect comparison to another COVID-19 drug. This is expected to allow the continued use of the subsequent entry drug to address shortages in Canada for the duration of the ISAD Interim Order, and to further allow a filing of the subsequent entry drug via Part C, Division 8 of the FDR while observing the existing filing restrictions, including data protection provisions.

To maintain the ability to sell, import or conduct other licensable activities related to a COVID-19 drug, manufacturers holding an authorization, as defined above, which was not suspended or revoked in whole, are required to submit an NDS or SNDS within

- ninety days following the coming into force of the amendments if the holder receives authorization prior to the regulatory amendments coming into force; or
- ninety days following issuance of an authorization under the ISAD Interim Order if the holder receives their authorization after the regulatory amendments come into force.

This 90-day period helps ensure the timely normalization of Interim Order authorizations, while providing a reasonable and equitable timeframe for all manufacturers to file an NDS under the FDR.

During the transition period, the DIN that was assigned under the Interim Order continues to be assigned to ensure that all regulatory obligations associated with it persist.

The transitional provisions require that an authorization under the ISAD Interim Order be revoked if

- an NOC is issued under the FDR for a drug authorized under the Interim Order while the Interim Order is in effect; or
- an NDS or SNDS submitted under the FDR for a drug that is authorized under the Interim Order does not meet the submission requirements and the authorization holder either does not provide additional information requested in the period specified by the Minister or the information that is provided is not sufficient and the Minister issues a notice to that effect under paragraph C.08.004(3)(b).

To prevent market lapse during the normalization of authorizations under the ISAD Interim Order, a manufacturer will be permitted to continue selling, within the scope of their authorization, the COVID-19 drug once the Interim Order ceases to have effect if

- they had received an authorization under the Interim Order;
- their authorization had not been revoked or suspended in whole when the Interim Order ceased to have effect; and
- they had the timelines for submission of an NDS or SNDS.

However, the manufacturer loses the right to sell if the Minister issued a notice that the submission does not meet the submission requirements and the authorization holder either did not provide the information requested within the period specified or the information was insufficient and the Minister issued a notice to that effect under paragraph C.08.004(3)(b).

If the holder of an Interim Order authorization is not able to file an NDS or an SNDS, as applicable, within the given timeline, the Interim Order authorization is revoked, and the manufacturer will have to wait until

receiving an NOC to continue sale.

For DELs, a holder whose DEL was issued or amended in respect of an Interim Order application must notify the Minister prior to the expiry of the ISAD Interim Order should they wish to maintain their authorized activities after it expires. Guidance documents will be updated to include considerations related to the notification process such as timelines and information to be included.

For pre-positioning, these amendments will deem information and material submitted under the ISAD Interim Order to be information and material submitted under the new paragraphs C.08.009.03(1)(a) and (b) and C.08.009.05(a).

Coming into force

Generally, amendments to the FDR related to the authorization pathways and associated submission flexibilities, including the modified safety and efficacy information requirements, rolling submissions, and terms and conditions are coming into force upon registration to provide certainty to manufacturers, to enable them to make use of the new pathways, and to help ensure the timely normalization of the ISAD Interim Order authorizations.

Most amendments relating to DEL, GMP, pre-positioning and other provisions relating to authorization pathways come into force upon expiry of the Interim Order, in order to not interrupt the framework established under the ISAD Interim Order.

Regulatory development

Consultation

These regulatory amendments directly impact the pharmaceutical industry and health care partners. It has a subsequent impact on Canadians by expediting authorization of, and access to COVID-19 drugs under the FDR.

Phase I – Stakeholder consultation

The policy intent of these amendments to the FDR included in this package was posted online for all stakeholders to provide comments between November 30, 2020, and December 21, 2020, and in addition, an email notification was sent out for this regulatory initiative. To facilitate the development of comments, Health Canada provided stakeholders with a set of questions for consideration.

On December 11, 2020, Health Canada hosted a targeted, interactive stakeholder webinar. Over 40 individuals from across the country participated in the webinar, representing the following groups: manufacturers who hold an ISAD Interim Order authorization, manufacturers who have applied for an Interim Order authorization, manufacturers who intend to apply for a COVID-19 drug authorization under the Interim Order or FDR, DEL holders, industry associations, pharmacist associations, hospital associations and provincial and territorial partners. Other relevant federal departments such as program leads from Innovation, Science and Economic Development Canada (ISED) and Patented Medicine Prices Review Board (PMPRB) supported Health Canada in this webinar.

The web-published notice and consultation document informed stakeholders and the general public of these amendments to the FDR and of the amendments to the *Fees in Respect of Drugs and Medical Devices Order*. Stakeholders provided verbal feedback in the webinar as well as written feedback following the webinar. A summary of “What Was Heard” is

published online and stakeholder feedback is addressed in the guidance document where appropriate. The feedback did not result in changes to the proposed amendments to the FDR.

Stakeholder feedback

Feedback was received through these consultations, and was part of one of the following categories:

- Suggestions to consider the need to retain key features of the ISAD Interim Order and transition provisions to ensure that the regulatory framework for human drugs is flexible enough to address any future pandemic. This is in line with the features retained, such as rolling submissions and flexibility on submission information in combination with the use of terms and conditions, which are included in this package. In general, there was positive consensus regarding the transition regulatory package as a whole, and strong support for the initiative to ensure an orderly normalization of drugs authorized under the Interim Order to the FDR. Health Canada will continue to work to modernize the framework and explore applying similar principles more broadly in future regulatory packages to address potential pandemics.
- The majority of comments requested clarification regarding submission filing procedures, the type and amount of information that would need to be filed, international harmonization and the extent of the Health Canada review of information previously reviewed under the Interim Order. These are addressed in the guidance document developed concurrently with the regulatory package to ensure stakeholders are well informed on procedure, process and timelines.
- Some stakeholders sought clarification regarding the timelines for transitioning an Interim Order authorization to an NOC under the FDR, and the amount of time that such a normalization would take. Health

Canada indicated that the 90-day period helps with a timely normalization of Interim Order authorizations, while providing a reasonable timeframe for all manufacturers to file an NDS under the FDR.

- Some comments regarding other measures that were part of Health Canada's response exceeded the scope of this package, such as the *List of Drugs for Exceptional Importation and Sale* referenced under the *Interim Order Respecting Drugs, Medical Devices and Foods for a Special Dietary Purpose in Relation to COVID-19*.
- Some industry stakeholders would prefer to have the submission flexibilities apply to SNDSs as well. Since such drugs are already authorized for other indications, and available on the market, with an established quality, safety and on-market experience, there is an expectation that much of the data is already available, including brand name assessments. Given that the data requirements are limited to the new indication, manufacturers are expected to file an SNDS without these flexibilities. Consequently, the submission flexibilities, as well as the ability to file rolling submissions are not applicable to such SNDSs.
- Comments were made around price assessment for patented COVID-19 drugs and stakeholders were referred to the applicable new PMPRB guidance document, available online.
- Comments were raised about how different types of foreign applications for marketing approval will be considered with respect to the “timely filing” of the Certificate of Supplementary Protection (CSP) requirement. Consideration of a foreign application for marketing approval continues to be governed by the existing language of paragraphs 106(1)(f) under the *Patent Act* and 6(1)(b) under the CSP

Regulations. Stakeholders are encouraged to consult the guidance document accompanying these amendments for further information.

- Stakeholders were supportive of continued flexibility for DEL applications and certain GMP requirements for COVID-19 drugs such as confirmatory testing. Some responses included additional challenges faced by industry with respect to GMP requirements, including sample retention requirements, annual product quality reviews, and maintenance of the stability program. While these measures are not within scope of the ISAD Interim Order or the amendments, Health Canada will consider these comments for future opportunities for regulatory flexibility.

Between November 30, 2020, and December 21, 2020, consultations on the guidance documents were conducted with manufacturers who hold an Interim Order authorization, manufacturers who have applied for an Interim Order authorization, manufacturers that have indicated they intend to apply for an authorization for a COVID-19 drug, and DEL holders.

Phase II – Stakeholder pre-implementation engagement

In anticipation of publication of these amendments in the *Canada Gazette*, manufacturers that held an authorization under the Interim Order were advised of these amendments and the need to apply for an authorization under the FDR. DEL holders were asked to provide notice of their intent to maintain any licensable activity that was added or amended through the ISAD Interim Order to avoid cancellation upon its expiry.

Further, during this period, Health Canada focused on advising stakeholders of their obligations and outlining for stakeholders how to normalize authorizations under the ISAD Interim Order to the FDR. As part

of Phase II, Health Canada is also publishing a guidance document to accompany the Regulations.

Phase III – Stakeholder support for implementation

Following the publication of these amendments in the *Canada Gazette*, Part II, and up until expiry of the ISAD Interim Order, Health Canada will continue to support manufacturers and DEL holders in providing information, and clarify obligations related to seeking an authorization under Division 8 of the FDR and compliance with establishment licensing and GMP requirements under Divisions 1A and 2, respectively. Health Canada may conduct webinars, as needed, with specific industry groups, or develop further information materials as needed.

This phase will occur for the duration of the transition period from the ISAD Interim Order and on an as-needed basis for new submissions. The focus of this phase will be to ensure that manufacturers have all of the information and support that they need in order to obtain authorization under Division 8 of the FDR. Health Canada may conduct webinars or product-specific pre-submission meetings or correspondence, as needed, with specific industry groups, or develop further information materials as needed.

Throughout all three phases of stakeholder engagement, in addition to consulting with manufacturers, Health Canada has sought feedback from health system partners, including the provinces and territories, as to how the Regulations should be applied. Health Canada will continue to hold these discussions as part of routine communications and meetings between Health Canada and the provinces and territories. Health Canada has also consulted with those groups within the federal government that are responsible for the procurement of drugs for the national stockpile.

Exemption of the proposal from prepublication

Health Canada sought an exemption from prepublication in the *Canada Gazette*, Part I, for these amendments in order to allow for a seamless transition and timely normalization, and to provide clarity and predictability to drug manufacturers and the health care system in relation to COVID-19 drugs authorized under the ISAD Interim Order, before its expiry.

These regulatory amendments and transitional regulatory provisions will provide manufacturers the regulatory authorization pathways to ensure continuity from the ISAD Interim Order. Given stakeholder familiarity with the ISAD Interim Order, Health Canada did not deviate significantly from the Interim Order in the drafting of this regulatory package. The burden placed on industry has been minimized by carrying over many of the flexibilities of the ISAD Interim Order.

Modern treaty obligations and Indigenous engagement and consultation

These amendments are not expected to have an impact on the Government's modern treaty obligations.

These amendments are intended to facilitate the importation or sale of drugs used in relation to COVID-19 in Canada for all Canadians, including Indigenous peoples.

As a result, it is expected that Indigenous peoples could receive an indirect benefit. If the Regulations do not proceed, disproportionately impacted groups may be more negatively impacted if the drugs authorized under the Interim Order cease to be available for import and sale. Specific consultations with Indigenous peoples were not undertaken.

Instrument choice

Health Canada considered the following regulatory and non-regulatory options.

Option 1: Status quo

In the status quo option, Health Canada would allow the ISAD Interim Order to expire without putting in place new regulations. Manufacturers of COVID-19 drugs would have to file a NDS under the existing FDR in order to obtain an NOC that would allow them to sell the drug after the Interim Order expired. However, without the flexibilities for COVID-19 drugs, it could take many years for a company to generate sufficient evidence to support an NDS. This would be in addition to the time required for the Minister to review the submission and issue an NOC authorizing the sale and advertisement of the drug. This could result in an unmet medical need or a market lapse of the drug.

Additionally, any regulated activities such as importation, fabrication or testing of a COVID-19 drug that was authorized by a DEL issued in respect of the ISAD Interim Order would no longer be authorized, as the DEL would be automatically cancelled when the Interim Order expired. Manufacturers might face challenges obtaining the necessary GMP evidence necessary to re-apply for the necessary DEL.

The status quo option was not deemed adequate to address the objectives given that COVID-19 is still a threat to public health at this time.

Option 2: Transition regulations

Under this option, Health Canada would develop new, temporary Governor in Council (GiC) regulations (separate from the FDR) that would include a similar scheme to be maintained as in the ISAD Interim Order. However, this option would not make use of the existing NOC framework outlined in Part C, Division 8 of the FDR. This transition would allow the continued sale of COVID-19 drugs authorized under the Interim Order, while providing manufacturers with more time to address post-market commitments, and gather information necessary to support a future NDS filing.

Furthermore, this option would only be temporary in nature, as all products would still need to be normalized into the existing FDR at a later time. This would delay normalization of the COVID-19 drugs, which would ultimately require similar FDR amendments as per Option 3 and would increase burden on industry, as they would have to transition twice. Additionally, since the data protection provisions, as well as the PMNOC Regulations and the CSP Regulations, are currently linked to the Division 8 framework, further amendments would potentially be needed to link them to the new GiC regulations.

Although Option 2 addresses the objectives, given the added complexities in comparison to Option 3, it was not the chosen option.

Option 3: Direct to FDR

The selected option transitions aspects of the ISAD Interim Order directly into the FDR by incorporating flexibilities related to market authorization (via the existing NDS and NOC pathway), drug establishment licensing, and pre-positioning of drugs. This would normalize the drug authorization process via the existing NDS and NOC pathway while allowing for the continued sale of COVID-19 drugs authorized under the ISAD Interim Order.

Option 3 addresses the objectives with the least complexity, and was therefore the chosen option.

Regulatory analysis

Benefits and costs

The amendments to the FDR allow for greater flexibility in dealing with an emergency that poses an immediate threat to the health of Canadians. These Regulations create greater flexibilities for industry in providing data and information to Health Canada in support of drug approvals as well as

maintain intellectual property rights. The baseline for the cost-benefit analysis is the standard authorization process found in the FDR. While the total costs cannot be exactly determined, as they are dependant on the duration of the pandemic and the number of products industry submits for review, they are estimated to be less than \$1 million per year. The quantified costs are borne mostly by Health Canada and the Public Health Agency of Canada. While there are costs to industry associated with the application of terms and conditions, the analysis below shows that they are not incremental to those that would normally be associated with the drug authorization process. In the event that industry were to determine that the incremental costs of the new flexibilities were too high, application for approval through the standard provisions in the FDR would still be possible.

The primary benefit of the Regulations is faster access for Canadians to drugs that prevent or treat COVID-19. The reduction in morbidity and mortality rates is impossible to estimate at this time. The amendments will also maintain the intellectual property rights of innovators and reduce burn time for firms. Burn time is the period between a drug being developed and when it begins to generate revenues by having been granted market authorization.

Incorporation of submission flexibilities into the NDS pathway

Manufacturers of a COVID-19 drug who are not able to fulfill the requirements of the NDS have access to submission flexibilities described in previous sections of this document. The benefit of these flexibilities to Canadians and industry is to reduce the time to market of COVID-19 drugs.

In addition, the requirement to provide mock ups of labels and packaging as well as a look-alike-sound-alike assessment was identified by industry during consultations for the 2014 *Regulations Amending the Food and Drug*

Regulations (Labelling, Packaging and Brand Names of Drugs for Human Use) as being both time consuming and costly by industry. The flexibilities around this requirement are anticipated to reduce costs for industry.

Incomplete submission and plan for information (rolling submissions)

The ability to file rolling submissions is designed to speed the approval process, as Health Canada will be able to review each piece of a submission when it becomes available, rather than having to wait for the entire package to be ready for review. The same information provided will be required, but the delivery of the submission information will be spread out over a longer period of time.

Industry indicated via survey responses that it does not believe that rolling submissions would add costs to their application. The regular NDS pathway already involves substantial back and forth when Health Canada seeks clarifications or newly found information must be communicated by industry to update a submission prior to its approval.

Health Canada estimates that these amendments will impose an average incremental cost of \$10,200 for vaccines and other COVID-19 – related drugs associated with the start-stop nature of rolling submissions, where data is submitted over time rather than as one package, as well as for the creation and review of any T&Cs that would be added to the market authorization (see the “Terms and conditions” section below). The costs are based on Health Canada's experience to date in reviewing vaccine and antiviral drug submissions, either under the ISAD Interim Order or the notice of compliance with conditions (NOC/c) policy.² Based on the number of potential vaccines and antivirals that could apply under the new flexibilities, Health Canada assumes that no more than five vaccines and

two antiviral drugs would apply for market access per year; the average incremental cost would be \$71,400, with an average cost of \$10,200 per product. These costs would be borne by Health Canada.

$$\text{Cost} = \$10,200 \times 7 = \$71,400$$

Terms and conditions

Vanessa's Law gave the Minister the power to impose terms and conditions on market authorizations through regulations. Prior to these amendments, the Vanessa's Law power has only been used to add T&Cs on the DINs of opioids. While Health Canada has had a long-standing policy that allows for a notice of compliance to be given with conditions, these amendments formalize the NOC/c policy into regulations for COVID-19 drugs, and allow for the imposition of T&Cs on a COVID-19 drug market authorization in order to resolve any uncertainties concerning the drug at the time of approval. The ISAD Interim Order contains provisions making the application of T&Cs binding on industry and these provisions are carried forward under the Regulations. In a typical NOC/c approval, only one or two conditions might be appended. For COVID-19 drugs under the ISAD Interim Order, the number of T&Cs has been much higher.

Due to the speed of development and review, T&Cs are more widely applied to COVID-19 drug approvals. Theoretically, they can range from low-cost activities, such as a leaflet to be handed out when a prescription is filled, to full Phase IV trials costing millions. The cost to industry could vary depending on the type of activities required, whether or not they are done in concert with other foreign regulators, whether or not there are requirements specific to Canada, and the capacity of the individual firm to do the activities. Industry identified T&Cs as potentially increasing cost beyond their perceived benefits of the package, in which case they would opt for the standard approval process.

Health Canada expects to only apply T&Cs that would help resolve any uncertainties about the drug and would provide Health Canada with the information that would normally be submitted for an NDS, provide data that Health Canada would typically receive voluntarily from industry because it is already provided to a foreign regulator (such as a periodic benefit-risk evaluation report [PBRER] required by the European Medicines Agency), or provide other studies and data that have been requested by international regulators to fulfil the terms of authorization. While a Canadian-only manufacturer would assume a significant cost, no such industry stakeholder is likely to seek approval under the normalization. Firms that operate internationally, which to date are the only ones identified, would only assume a marginal cost of forwarding the exact same information to Health Canada. Assuming \$100 in the cost of writing and approving an email to forward the report, and assuming five such reports per drug, a manufacturer would spend \$500 per year, per drug. Based on the number of drugs for which Health Canada believes approval would be sought (seven drugs per year), the cost would be \$3,500 to industry.

$$\text{Cost} = \$100 \times 5 \times 7 = \$3,500$$

In addition to the costs to Health Canada identified above for the approval of a rolling submission and some of the activities around T&Cs, Health Canada anticipates an additional \$265,783 in costs for post-market activities. This incremental cost to Government is based on the need to add an additional two staff members to deal with the increased volume of data that is anticipated to be received after approval to monitor real world safety and effectiveness of COVID-19 drugs. The data to fulfill the T&Cs may be submitted depending on when it becomes available, which may extend over a period of time longer than one year.

Good manufacturing practices

The amendments introduce an exception to periodic confirmatory testing requirements in subsections C.02.019(1) and (2) when a request has been made by the Minister under section C.04.015 (lot release). This amendment addresses a known irritant within the biologic drug industry, by reducing burden associated with testing when the drug is subject to Health Canada's lot release program.

This exception decreases the testing requirements for a subset of products. One industry stakeholder estimated that not sending samples for testing would lead to cost savings totalling between \$40,000 and \$50,000 per drug. Assuming the savings would be uniform to all COVID-19 drug manufacturers and importers and assuming seven drugs per year, the total cost savings could be as high as \$315,000. At present, it is unclear how many drugs would not already be exempt from this requirement; therefore, the savings are likely to be far less.

Drug establishment licensing

The amendments allow the continued operation of establishments without disruption.

The Regulations do not introduce any additional requirements for applicants or DEL holders in respect of a COVID-19 drug when compared to the requirements of the FDR, and therefore, no additional costs result from these Regulations.

Pre-positioning

Health Canada and the Public Health Agency of Canada expect that no more than two drugs would be pre-positioned per year. Industry does not anticipate bearing incremental costs for pre-positioning. The cost to

Government is estimated to be \$11,109 for Health Canada and \$506 for PHAC per drug. Assuming two drugs, the total cost to Government would be \$23,230.

$$\text{Cost} = (\$11,109 + \$506) \times 2 = \$23,230$$

Intellectual property

As a consequence of the amendments to the FDR, manufacturers may benefit from intellectual property protections that are available in the standard approval process under the FDR. In the technical sense, this would neither be a cost nor a benefit of the Regulations, as the baseline for analysis is the standard approval process.

Total quantified costs and benefits

Assuming the costs identified above are borne each year for seven drugs, the total quantifiable costs are estimated to be \$363,913 for each year the interim regulatory regime is in place. The total quantified benefits are estimated to be \$45,000 per drug that is exempt from testing. Given the uncertainties regarding the duration and severity of the pandemic, and the number of drug submissions that may be received by Health Canada in future years, these results could vary significantly. However, in all cases, companies would have the option to take normal approval pathways under the FDR, and Health Canada would maintain the option for adding terms and conditions when issuing an NOC.

Small business lens

The small business lens does not apply, as no firms that fit the definition of a small business (i.e. a business with fewer than 100 employees or less than \$5 million in revenue) are expected to use the flexibilities in these regulatory amendments.

One-for-one rule

Health Canada is seeking an exemption from the one-for-one rule, as these Regulations address an imminent danger to human health. They therefore meet the criteria for an exemption to the *Red Tape Reduction Act* for regulations in an emergency or exceptional circumstance provided for in the *Red Tape Reduction Regulations*.

Industry indicated in its consultation responses that it did not believe the Regulations imposed any additional administrative costs. While data provided in support of a drug approval is not considered to be “administrative burden,” reporting requirements after approval are included in the rule. The use of T&Cs, therefore, would be construed to add administrative burden. Given the manner in which T&Cs were applied under the ISAD Interim Order and Health Canada's intention for applying them under the amendments, Health Canada estimates that the administrative burden will be limited to the forwarding of information, data, and reports that are already generated for other regulators. The cost is anticipated to be \$100 per report submitted five times per year per drug, for seven drugs, for a total of \$3,500 (2021\$). For the purpose of the one-for-one rule, real values as measured at 2012 price levels are used and the cost is \$89 (2012\$) per report. Assuming the COVID-19 amendments are used only for one year, the cost for the purpose of the requirement is summarized in the table below. If the pandemic were to last longer and authorization was to be sought for additional products under these Regulations, the administrative burden would be higher.

Table 1: Summary of annualized administrative costs

Description of cost	Amount
Annualized administrative costs	\$232

Annualized administrative costs per business	\$33.10
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Regulatory cooperation and alignment

Health Canada is working with our international partners on a coordinated and well-aligned approach to respond to the COVID-19 pandemic. Health Canada is playing a leadership role in helping align policy approaches and regulatory agility, which involves discussing, collaborating and leveraging resources on issues related to

- clinical trials and investigational testing;
- drug and medical device market authorizations;
- health product risk assessments;
- potential drug and medical device shortages.

Furthermore, Health Canada participates in

- the International Coalition for Medicines Regulatory Authorities (ICMRA) as an executive committee member, and plays a leadership role in aligning policy approaches and regulatory agility;
- the World Health Organization's research and development blueprint (R&D Blueprint) plan to develop a COVID-19 vaccine; and
- the Pan American Health Organization as a member of its COVID-19 task group.

This regulatory package will ensure that access to COVID-19 drugs is maintained following the expiration of the ISAD Interim Order. It also ensures continuity in the post-market oversight and collection of information with respect to the safety and efficacy of these drugs. Other comparable foreign authorities have emergency pathways in place that

enable them to provide access to COVID-19 drugs to their populations on an expedited basis using limited information respecting a drug, compared to their full authorization pathways.

The United States

The United States has an Emergency Use Authorization (EUA) that enables the Food and Drug Administration (FDA) Commissioner to allow unapproved products or unapproved uses for authorized products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases when there is a declaration of a public health emergency and there are no adequate approved and available alternatives. The EUA is not a separate pathway, it is an authorization that may be received while data is being collected to support licensure. Products that are granted an EUA are generally in the process of undergoing clinical trials, with licensure being pursued under one of the available pathways.

Products that are granted an EUA will continue to be authorized under this pathway with the terms placed on their authorization until the declaration of emergency is terminated or the authorization is revoked.

European Union

The European Union regulations provide its members with the authority to conduct rolling submissions and recommend products for conditional marketing authorization to facilitate early access to medicines that fulfill an unmet medical need, including in response to a public health emergency. It allows for the issuance of a market authorization with less complete data if the benefit of the medicine's immediate availability to patients outweighs the risks. Conditions are placed on the authorization requiring that the authorization holder submit post-market data with respect to safety and effectiveness. A risk management plan is also a requirement to ensure

post-market safety monitoring. A conditional marketing authorization is valid for one year and is renewable. It may also be suspended or revoked at any time should the benefit-risk balance become negative or the company not comply with specific obligations.

When all specific obligations have been completed, if the positive benefit-risk balance of the product is confirmed, the authorization is converted into a standard marketing authorization.

Australia

Implemented in 2018, the provisional approval pathway facilitates earlier access to medicines that address unmet clinical needs for Australian consumers without compromising safety, efficacy and quality. The provisional approval pathway enables a time-limited registration of a promising drug, based on preliminary (usually Phase II) clinical data. If approved, the drug will be available for two years and the drug's sponsor can apply for extensions up to a total of six years. Registration will automatically lapse at the end of a specified period unless sponsors are able to demonstrate that they have met the conditions imposed on the provisional registration. Successful evaluation of this confirmatory data will result in a transition to full registration on the Australian Register of Therapeutic Goods. The initial provisional approval and continuing registration are only permitted if the Therapeutic Goods Administration (TGA) is satisfied that confirmatory data will be submitted within six years. Sponsors may apply for full registration when sufficient clinical data to confirm the safety and efficacy of the medicine is available.

United Kingdom

The Early Access to Medicine Scheme (EAMS) in the United Kingdom (U.K.) facilitates earlier access to drugs that do not yet have a marketing authorization when there is a clear unmet medical need. The pathway requires that the condition the drug is intended to treat be life threatening or seriously debilitating, that the product be likely to offer a major advantage over the approved medications currently available in the U.K., and that there be a positive benefit-risk balance. The Medicines and Healthcare products Regulatory Agency (MHRA) will give a scientific opinion on the benefit-risk balance of the medicine, based on the data available when the EAMS submission was made. It supports the patient and prescriber in making a decision on whether to use the medicine before its licence is approved. Once a sponsor has been granted a positive EAMS scientific opinion, they must provide the MHRA with regular updates at an agreed-upon frequency.

Health products approved under EAMS must meet the requirements of the full drug licensing pathway in order to transition to a market authorization.

Strategic environmental assessment

Environmental impacts have not been identified for this regulatory package; therefore, a detailed analysis was not warranted.

Gender-based analysis plus

COVID-19 was found to have various direct and indirect socioeconomic and health-related impacts on the genders, in addition to other Canadian demographics. Factors affecting vulnerability to the disease included individual conditions (e.g. increased age, pre-existing medical conditions), social conditions (e.g. lower socioeconomic status, residence in long-term care facilities or crowded/remote locations, homelessness, substance use

disorder, race/ethnicity, immigration or refugee status), and occupational conditions (e.g. health care workers, emergency workers, workers who have a high degree of social contact, international business travellers). ³

For example, when the Government of Ontario announced a state of emergency in March 2020 that resulted in the closure of non-essential businesses, twice as many women between the ages of 25 and 54 were left unemployed as men. For those who remain employed, challenges related to childcare have been encountered. In most provinces, a limited supply of licensed childcare options has often led to one parent, normally the mother, having to abandon their employment. ⁴

Gender-specific impacts also included women having to travel out of province for abortions because hospitals sidelined or cancelled all procedures at their local hospitals. These inter-provincial trips have also been impossible at times due to travel restrictions imposed by various provincial jurisdictions during the pandemic. ⁵

Socioeconomic aspects show that people living in poverty or earning lower incomes were more impacted than those with a higher income. Some examples include homeless people forced from parks with no place to go, ⁶ shelters deemed to be unsafe, ⁶ less access to health care, ⁷ unstable employment, ⁷ and less ability to stockpile food and other cleaning supplies. ⁷ According to an article in the *Canadian Medical Association Journal*, Indigenous communities may be at greater risk of developing severe symptoms and dying of COVID-19, given the lack of access to clean water and limited health infrastructure that lead to an increased presence of overcrowding, making social distancing difficult. Other socioeconomic considerations could also impact Indigenous communities. ⁸ COVID-19

infection rates and deaths are sensitive to variables like income, employment, housing, and language, which are frequently present to varying degrees in Indigenous communities.

Based on data reported up to December 18, 2020, the largest bias for all Canadians is the impact of age or other health conditions on the severity of the disease. Throughout all the COVID-19 cases in Canada, individuals aged 60 years and over account for just over 96% of deaths attributed to the virus.⁹

These regulatory amendments are expected to benefit all Canadians by enabling continuity in market access to COVID-19 drugs and drugs with COVID-19 indications. The regulatory amendments are expected to have a positive effect on certain groups, particularly those that are most vulnerable to COVID-19. If the Regulations do not proceed or manufacturers choose not to normalize their authorizations, disproportionately impacted groups may be more negatively impacted with the drugs authorized under the ISAD Interim Order becoming inaccessible.

Implementation, compliance and enforcement, and service standards

Implementation

Health Canada will reach out to stakeholders to support them in the implementation of these Regulations as outlined in Phase III — Stakeholder support for implementation of the “Consultation” section of this document.

Additionally, to support the implementation of the transition of COVID-19 drugs to the FDR, Health Canada is adapting the *Information and application requirements for drugs authorized under the Interim Order: Guidance*

document, aimed to be published concurrently with new amendments to the FDR, to provide the FDR context.

Given that the amendments to the FDR related to DEL applications for COVID-19 drugs come into force when the ISAD Interim Order expires, applicants submitting a DEL application in relation to a COVID-19 drug should continue to follow the above-mentioned guidance.

In addition, stakeholder information sessions and discussions during bilateral meetings with industry and industry stakeholder groups will provide other opportunities to directly engage with stakeholders regarding COVID-19 drugs and these regulatory requirements.

Transparency will continue on Canada.ca to communicate up-to-date information concerning incoming submissions and other materials related to COVID-19 drugs that are now being transitioned to the *Food and Drug Regulations*.

Through their interdepartmental collaborative efforts, Health Canada, PHAC, Innovation, Science and Economic Development Canada, and Public Services and Procurement Canada will continue to ensure that the linkages to other policy objectives, such as pre-positioning, are implemented effectively. PHAC continues to work with provincial and territorial partners to support coordination for the efficient distribution of promising COVID-19 drugs, once they are authorized.

Compliance and enforcement

Compliance and enforcement of the Regulations will be in accordance with a risk-based approach, aligned with existing departmental policies, including compliance promotion and monitoring and enforcement activities in accordance with Health Canada's *Compliance and enforcement policy for health products (POL-0001)*. All terms and conditions, including

those that apply to DELs, will be enforceable under section 21.7 of the Act. Failure to comply with terms and conditions could result in Health Canada taking compliance and enforcement action. The type of action would be determined in accordance with Health Canada's policy and depend on the nature of the contravention, and could result in the partial cancellation or the suspension of the licence or market authorization.

Health Canada recognizes the impact a pandemic can have on the pharmaceutical industry. A number of interim measures have been implemented since the beginning of the pandemic, providing regulatory flexibility for DELs and GMP. These measures are not limited to COVID-19 drugs, but apply to all drugs that may have been impacted by the pandemic.

Service standards

Health Canada will continue to prioritize submissions related to COVID-19 until such time as the disease no longer represents a public health emergency. In addition, the review of those submissions will be expedited where possible in comparison to the existing service standards set out in the document *Performance Standards for the Fees in Respect of Drugs and Medical Devices Order*, published by the Government of Canada.

DEL applications in relation to a COVID-19 drug will be prioritized and reviewed in an expedited fashion. The time that it will take to complete the review will depend on the application itself, the volume of evidence to be assessed and the number of applications received. The performance standards in *Service Standard for Drug Establishment Licences under the Food and Drug Regulations* do not apply to these Regulations.

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Footnotes

- a S.C. 2020, c. 5, s. 33
- b R.S., c. F-27
- 1 C.R.C., c. 870
- 2 An NOC/c is a policy in which Health Canada grants an NOC to a drug taking into account a commitment from the authorization holder to fulfill certain post-market activities requested by the Health Canada to resolve uncertainties regarding the drug.
- 3 National Advisory Committee on Immunization (NACI). "Preliminary guidance on key populations for early COVID-19 immunization" (2020).

- 4 Ontario Chamber of Commerce. "The She-covery Project: Confronting the Gendered Economic Impacts of COVID-19 in Ontario (PDF)".
 - 5 Osman, Laura. "Advocates sound alarm over COVID-19 limiting access to contraceptives, abortion"; The Canadian Press (2020).
 - 6 Bains, Camille. "Homeless vulnerable to COVID-19 need help from governments: advocates"; The Canadian Press (2020).
 - 7 Public Health Agency of Canada. "Coronavirus disease (COVID-19) – Vulnerable populations and COVID-19".
 - 8 Banning, Jolene. "Why Indigenous communities seeing few cases of COVID-19"; Canadian Medical Association Journal (2020).
 - 9 Government of Canada, Infobase Canada. "Coronavirus disease 2019 (COVID-19): Epidemiology update".
-